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WORKING MEMORY AND REFERENCE MEMORY IN ADULT RATS FOLLOWING LIMBIC SEIZURES INDUCED AT 21 OR 90 DAYS OF AGE[1]

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Summary.—Rats were either seized or not seized at 21 days of age (weaning) or at 90 days of age with a single systemic injection of lithium (3 mEq/kg) and pilocarpine (30 mg/kg). When tested as adults (120 days of age) for spatial memory in the Olton radial maze, the rats that had been seized as adults exhibited about five times more working (short-term) memory errors than the other three groups which did not differ significantly from one another. The numbers of errors for long-term (reference) memory did not differ significantly among the four groups. The deficits in working memory for the group seized as weanlings and reported previously were not replicated. One possible explanation for this discrepancy might be differential effects upon brain organization associated with seizures evoked by injecting the pilocarpine 24 hr. rather than 4 hr. after the lithium.

Kostakos, Persinger, and Peredery (1993) reported that rats in which limbic seizures had been induced before weaning exhibited deficits in working memory but not in reference memory for a spatial task. The present study was designed to extend this research by testing adult rats that had been seized before weaning and directly comparing them to same-age, litter mates seized as adults.

Method.—A total of 32 male and female Wistar albino rats from four different litters (that had been culled to four male and four female pups at two days of age) were subjects. On the day of weaning eight rats were seized by a subcutaneous injection of 3 mEq/kg of lithium chloride followed 24 hr. later by 30 mg/kg of pilocarpine. Another eight rats were injected with saline. Immediately following the second injection, each rat was injected subcutaneously with 30 mg/kg of acepromazine. When the other 16 rats had reached 90 days of age eight of these rats were injected with 3 mEq/kg of lithium, followed 24 hr. later by 30 mg/kg of pilocarpine, and then within 30 min. after the seizure with 30 mg/kg of acepromazine. The other eight rats were controls. The rationale for this procedure was published elsewhere (Persinger, Bureau, Kostakos, Peredery, & Falter, 1993).

Consequently there were four groups with eight rats per group. When the rats were 120 days old, they were housed singly and maintained on a 23-hr. food deprivation schedule. After three days of adaptation, each rat was tested each day for 10 successive days in an Olton Maze. The same four arms of the eight arms were always baited with food (2 fruit loops), while the other four arms were never baited. Each session was no longer than 15 min. and was followed by 1 hr. of opportunity to consume (Purina) rat chow. Water was available *ad libitum*. All rats were housed singly during the experiment.

Seven rats were excluded from the analyses because they did not acquire the task. The final sample included seven of the 21-day control, eight of the 21-day seized, six of the 90-day

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controls, and four of the 90-day seized rats. The ratio of males and females was similar for each group. Reference errors were defined as the number of times per session the rat entered an arm that had never been baited. Working errors were defined as the number of times per session the rat re-entered an arm in which it had received reinforcement on that day. The mean numbers of errors for reference and for working memory per day for the 10 sessions were analyzed as a function of treatment and age at the time of treatment.

Results.—The means and standard errors of the mean for the numbers of errors for working memory and reference memory per day for the groups were for the 21-day controls 3.0 ($SE=0.5$), 2.8 ($SE=0.6$); 21-day seized 2.1 ($SE=0.3$), 2.2 ($SE=0.1$); 90-day control 4.0 ($SE=1.1$), 2.1 ($SE=0.2$); 90-day seized: 10.1 ($SE=3.8$), 2.3 ($SE=0.1$), respectively. Given the absence of main effects for sex and the small sample, sex of rat was ignored. A three-way analysis of variance with one factor repeated (working vs reference) and two between-subject factors (age; seizure) yielded a significant ($F_{1,21}=9.04$, $p<.01$; $\eta^2=30\%$ of the variance) interaction between age and treatment and type of memory. It was responsible for the main effect for type of memory ($F_{1,21}=16.83$, $p<.001$) and the two-way interactions between treatment and type of memory ($F_{1,21}=5.29$, $p<.05$) and age by type of memory ($F_{1,21}=15.77$, $p<.01$).

The greater deficits in working memory for rats seized as adults and tested as adults were similar to previous results (Persinger, *et al.*, 1993). However, we did not replicate the results of Kostakos, *et al.* (1993) which showed rats seized around weaning displayed more errors of working (short-term) memory when tested as adults. One procedural difference between the present and past studies was the interval (24 hr. vs 4 hr.) in administration of lithium and pilocarpine. Although these temporal discrepancies do not appear to affect adult deficits, the seizures induced following these two latencies may differentially influence the developing brain.

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